

### AMENDMENTS TO THE CLAIMS

1. (Currently amended) A precursor molecule of the formula  
[MABB-(AA)<sub>n</sub>-NuBB], wherein  
MABB is a masked aldehyde building block of the formula:  
[MA-L<sub>1</sub>-AG-], wherein  
MA is a masked aldehyde,  
L<sub>1</sub> is an aryl or alkyl comprising x covalently linked atoms selected from the group consisting of C, N, O and S, wherein x is an integer in the range of 0 to 10, and wherein said aryl ring or alkyl chain may be substituted independently on each position, and wherein the atom most proximal to the CO group is a carbon atom,  
AG is an acidic group capable of forming an amide bond,  
AA is an amino acid of the formula -NHCR<sup>1</sup>R<sup>2</sup>CO- and n is an integer in the range of 0 to 5,  
NuBB is a nucleophile building block of the formula  
[-NH-L<sub>2</sub>-Nu-], wherein  
-NH is an amino group that form the amide bond with AA or when n is 0 with AG,  
L<sub>2</sub> is an alkyl comprising in the range of 1 to 4 covalently linked atoms selected from the group consisting of C, N, O and S, wherein each atom may be independently substituted,  
Nu is a nucleophilic chemical entity comprising a π system, comprising an N, O or S atom or a chemical entity which is substituted with an N, O or S atom[[.]],  
wherein NuBB is linked to (AA)<sub>n</sub> or if n=0 to MABB via an amide bond and with the proviso, that when x=0, then n is at least 1,  
and wherein the masked aldehyde may be transformed into a free aldehyde, and the free aldehyde group is capable of interacting intramolecularly with an amide group, thereby forming an N-acyliminium ion,

and wherein said N-acyliminium ion is capable of acting as an electrophile for intramolecular reaction with said nucleophilic chemical entity,

and wherein said precursor molecule is attached to a solid support.

2. (Original) The precursor according to claim 1, wherein the nucleophilic chemical entity is capable of participating in a Pictet-Spengler reaction, or a cyclization process involving a electronrich double or triple bond to form a new covalent bond, thereby forming a heterocyclic organic compound comprising at least 2 fused rings designated A and B, wherein ring A incorporates a carbonyl group and ring A and B shares at least one N atom.

3. (Cancelled)

4. (Original) The precursor according to claim 1, wherein the nucleophile chemical entity is selected from the group consisting of mono-, di- and trisubstituted aromatic and heteroaromatic rings, alkenes and alkynes comprising N, S or O.

5. (Original) The precursor according to claim 1, wherein the nucleophilic chemical entity is selected from the group consisting of arenes, benzothiophene, benzofuran, isoindoles, 1,3-azole, imidazole, thiazole, oxazole, 1,2-azole, pyrazole, isothiazole, isoxazole, isoxazoline, purine, indolizine, quinolizine, pyrrolizine, 1,2,3-triazole, 1,2,4-triazole, pyridine, quinoline, isoquinoline, pyridazine, pyrimidine, pyrazine, pyrrole, indole, thiophene and furane.

Claims 6-12 [Cancelled]

13. (Currently amended) The precursor according to claim 1, wherein the masked aldehyde is protected by an aldehyde protecting group is selected from the group consisting of N-Boc N,O-acetals, di-Boc N,N-acetals, N-Boc N,S-acetals, di-O-acetals, di-S-acetals, S,O-acetals, F-moc and trialkylsilyl.

14. (Cancelled)

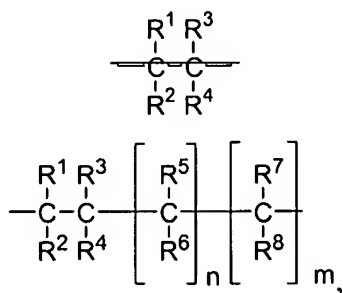
15. (Original) The precursor according to claim 1, wherein the masked aldehyde has the formula  $-\text{CO}-\text{X}$ , wherein X is not  $-\text{H}$ .

Claims 16-25 [Cancelled]

26. (Original) The precursor according to claim 1, wherein  $\text{L}_1$  is an alkyl chain.

27. (Cancelled)

28. (Currently amended) The precursor according to claim 1, wherein  $\text{L}_1$  has the structure



wherein  $n$  is 0 or 1 and  $M$  is 0 or 1 and wherein  $\text{R}^1, \text{R}^2, \text{R}^3, [\text{and}] \text{R}^4, \text{R}^5, \text{R}^6, \text{R}^7$  and  $\text{R}^8$  independently may be selected from the group of functionalities consisting of H, hydroxy, alkoxy, aryloxy, acyloxy, thiol, alkylthio, arylthio, heteroarylthio, sulphonyl, sulphoxy, amino, alkylamino, dialkylamino, acylamino, diacylamino, alkoxycarbonylamino, amides, alkyl, branched alkyl, aryl, heteroaryl, nitro, cyano, halogeno, silyloxy, keto, heterocycles, fused ring systems, fused heterocycles and mixtures thereof, wherein each of the aforementioned may be substituted with one or more groups selected from the group consisting of  $-\text{H}$ ,  $-\text{OH}$ ,  $-\text{SH}$ , halogen, carboxyl, carbonyl, alkoxy, aryloxy, acyloxy, alkylthio, arylthio, heteroarylthio, sulphonyl, sulphoxy, amino, alkylamino, dialkylamino, acylamino, diacylamino, alkoxycarbonylamino, amides, alkyl, aryl, heteroaryl, nitro, cyano, halogeno, silyloxy, keto, heterocycles, fused ring systems, and fused heterocycles.

Claims 29-36 [Cancelled]

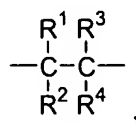
37. (Original) The precursor according to claim 1, wherein the acidic group is selected from the group consisting of -CO (carbonyl), -CS, -SO<sub>2</sub>H, -SO<sub>3</sub>H, -PO<sub>2</sub>H and -PO<sub>3</sub>H.

38. (Original) The precursor according to claim 1, wherein the amide group is selected from the group consisting of carbonyl amide, thiocarbonyl amide, phosphinic amide, phosphonic amide, sulfonic acid amide and sulfinic acid amide.

39. (Original) The precursor according to claim 1, wherein AA is an amino acid selected from the group consisting of naturally occurring amino acids, unnatural  $\alpha$ -amino acids, and unnatural  $\beta$ -amino acids.

40. (Cancelled)

41. (Original) The precursor according to claim 1, wherein L<sub>2</sub> has the structure



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> independently may be selected from the group consisting of H, hydroxy, alkoxy, aryloxy, acyloxy, thiol, alkylthio, arylthio, heteroarylthio, sulphonyl, sulphony, amino, alkylamino, dialkylamino, acylamino, diacylamino, alkoxycarbonylamino, amides, alkyl, branched alkyl, aryl, heteroaryl, nitro, cyano, halogeno, silyloxy, keto, heterocycles, fused ring systems, fused heterocycles and mixtures thereof, wherein each of the aforementioned may be substituted with one or more groups selected from the group consisting of -H, -OH, -SH, halogen, carboxyl, carbonyl, alkoxy, aryloxy, acyloxy, alkylthio, arylthio, heteroarylthio, sulphonyl, sulphony, amino, alkylamino, dialkylamino, acylamino, diacylamino,

alkoxycarbonylamino, alkyl, branched alkyl, aryl, heteroaryl, nitro, cyano, halogeno, silyloxy, keto, heterocycles, fused ring systems, and fused heterocycles.

Claims 42-56 (Cancelled)

57. (Original) The precursor according to claim 1, wherein the solid support is a resin bead comprising polyethylene glycol (PEG).

58. (Cancelled)

59. (Currently amended) A method of preparing a precursor molecule according to ~~any of~~ claims 1 to 58, comprising the steps of

i) Providing a masked aldehyde building block (MABB) of the formula:  
[MA-L<sub>1</sub>-AG<sub>2</sub>], wherein

MA is a masked aldehyde protected by an aldehyde protecting group,

L<sub>1</sub> is an aryl or alkyl comprising x covalently linked atoms selected from the group consisting of C, N, S and O that may be substituted independently on each position, wherein x is an integer in the range of 1 to 10 wherein the atom most proximal to the CO group is a carbon atom,

AG<sub>2</sub> is an acidic group capable of reacting with an amino group to form an amide,

ii) Providing a molecule of the structure [-(AA)<sub>n</sub>-NuBB], wherein

AA is an amino acid and n is an integer in the range of 0 to 5,

NuBB is a nucleophile building block of the formula

[-NH-L<sub>2</sub>-Nu-], wherein

-NH- is the amino group that form an amide bond with AA or when n is 0

-NH- is an -NH<sub>2</sub> group capable of forming an amide with AG<sub>2</sub>,

L<sub>2</sub> is an alkyl comprising in the range of 1 to 4 covalently linked atoms selected from the group consisting of C, N, O and S, wherein each atom may be independently substituted,

Nu is a nucleophilic chemical entity comprising a  $\pi$  system comprising an N, O or S atom or a chemical entity which is substituted with an N, O or S atom, wherein (AA)<sub>n</sub> is linked to NuBB via an amide bond, and wherein said molecule is covalently attached to a solid support

- iii) Reacting said MABB with said molecule, thereby forming an amide bond between said MABB and said molecule
- iv) Thereby obtaining a precursor molecule.

Claims 60-61 [Cancelled]

62. (Original) The method according to claim 59, wherein said nucleophilic chemical entity is selected from the group consisting of chemical entities comprising a functional group selected from the group consisting of -NHR, -NH<sub>2</sub>, Alkyl-SH, Aryl-SH, Alkyl-OH, Aryl-OH, mono-, di-, and trisubstituted aromatic and heteroaromatic rings, alkenes and alkynes.

Claims 63-66 (Cancelled)

67. (Currently amended) The method according to claim ~~59~~ 65, wherein the masked aldehyde is protected by an aldehyde protecting group is selected from the group consisting of N-Boc N,O-acetals, di-Boc N,N-acetals, N-Boc N,S-acetals, N-F-moc N,O-acetals, di-F-moc N,N-acetals, N-F-moc N,S-acetals, [[of]] N-triakylsilyl N,O-acetals, di-triakylsilyl N,N-acetals, N-triakylsilyl N,S-acetals, di-O-acetals, di-S-acetals and S,O-acetals.

68. (Cancelled)

69. (Original) The method according to claim 59, wherein the protected aldehyde has the formula -CO-X, wherein X is not -H.

Claims 70-71 (Cancelled)

72. (Original) The method according to claim 59, wherein L<sub>1</sub> is an alkyl chain.

Claims 73-74 (Cancelled)

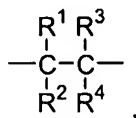
75. (Original) The method according to claim 59, wherein AG<sub>2</sub> is selected from the group consisting of carboxylic acid, carboxylic acid halogenid, sulfonyl halogenid and phosphonyl halogenid.

76. (Original) The method according to claim 59, wherein the amide is selected from the group consisting of carbonyl amide, thiocarbonyl amide, phosphinic amide, phosphonic amide, sulfonic acid amide and sulfinic acid amide.

77. (Original) The method according to claim 59, wherein AA is an amino acid selected from the group consisting of naturally occurring amino acids, unnatural  $\alpha$ -amino acids, and unnatural  $\beta$ -amino acids.

78. (Cancelled)

79. (Original) The method according to claim 59, wherein L<sub>2</sub> has the structure



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> independently may be selected from the group consisting of H, hydroxy, alkoxy, aryloxy, acyloxy, thiol, alkylthio, arylthio, heteroarylthio, sulphonyl, sulphoxy, amino, alkylamino, dialkylamino, acylamino, diacylamino, alkoxycarbonylamino, amides, alkyl, branched alkyl, aryl, heteroaryl, nitro, cyano, halogeno, silyloxy, keto, heterocycles, fused ring systems, fused heterocycles and mixtures thereof, wherein each of the aforementioned may be substituted with one or more groups selected from the group consisting of -H, -OH, -SH, halogen, carboxyl, carbonyl, alkoxy, aryloxy, acyloxy, alkylthio, arylthio, heteroarylthio, sulphonyl, sulphoxy, amino, alkylamino, dialkylamino, acylamino, diacylamino,

alkoxycarbonylamino, alkyl, branched alkyl, aryl, heteroaryl, nitro, cyano, halogeno, silyloxy, keto, heterocycles, fused ring systems, and fused heterocycles.

Claims 80-81 [Cancelled]

82. (Currently amended) A method of preparing a heterocyclic organic compound comprising at least 2 fused rings designated A and B, wherein ring A incorporates a carbonyl group and ring A and B shares at least one N atom, said method comprising the steps of

a) Providing a precursor molecule of the formula:

[MABB-(AA)<sub>n</sub>-NuBB], wherein

MABB is a masked aldehyde building block of the formula:

[MA-L<sub>1</sub>-AG-], wherein

MA is a masked aldehyde,

L<sub>1</sub> is an aryl or alkyl comprising x covalently linked atoms selected from the group consisting of C, N, O and S, wherein x is an integer in the range of 0 to 10, and wherein said aryl ring or alkyl chain may be substituted independently on each position, and wherein the atom most proximal to the CO group is a carbon atom,

AG is an acidic group capable of forming an amide bond,

AA is an amino acid of the formula -NHCR<sup>1</sup>R<sup>2</sup>CO- and n is an integer in the range of 0 to 5,

NuBB is a nucleophile building block of the formula

[-NH-L<sub>2</sub>-Nu-], wherein

-NH is an amino group that form an amide bond with AA or when n is 0 with AG,

L<sub>2</sub> is an alkyl comprising in the range of 1 to 4 covalently linked atoms selected from the group consisting of C, N, O and S, wherein each atom may be independently substituted,

Nu is a nucleophilic chemical entity comprising a π system,



wherein NuBB is linked to (AA)<sub>n</sub> or if n=0 to MABB via an amide bond and with the proviso, that when x=0, then n is at least 1,

and wherein the masked aldehyde may be transformed into a free aldehyde, and the free aldehyde group is capable of interacting intramolecularly with an amide group, thereby forming an N-acyliminium ion,

and wherein said N-acyliminium ion is capable of acting as an electrophile for intramolecular reaction with said nucleophilic chemical entity,

and wherein said precursor molecule is attached to a solid support[[]],

b) Transforming the masked aldehyde into a free aldehyde

c) Reacting said free aldehyde with an amide group within said precursor molecule, thereby obtaining an N-acyliminium ion, wherein said N-acyliminium ion is capable of acting as an electrophile

c) Performing an intramolecular nucleophilic reaction involving the N-acyliminium ion and the nucleophilic chemical entity forming a new covalent bond, thereby obtaining said cyclic organic compound.

83. (Currently amended) The method according to claim 82, wherein the precursor molecule is ~~the precursor molecule according to any of claims 1 to 58.~~ of the formula

[MABB-(AA)<sub>n</sub>-NuBB], wherein

MABB is a masked aldehyde building block of the formula:

[MA-L<sub>1</sub>-AG-], wherein

MA is a masked aldehyde,

L<sub>1</sub> is an aryl or alkyl comprising x covalently linked atoms selected from the group consisting of C, N, O and S, wherein x is an integer in the range of 0 to 10, and wherein said aryl ring or alkyl chain may be substituted independently on each position, and wherein the atom most proximal to the CO group is a carbon atom,

AG is an acidic group capable of forming an amide bond,

AA is an amino acid of the formula -NHCR<sup>1</sup>R<sup>2</sup>CO- and n is an integer in the range of 0 to 5,

NuBB is a nucleophile building block of the formula

[-NH-L<sub>2</sub>-Nu-], wherein

-NH is an amino group that form the amide bond with AA or when n is 0 with AG,

L<sub>2</sub> is an alkyl comprising in the range of 1 to 4 covalently linked atoms selected from the group consisting of C, N, O and S, wherein each atom may be independently substituted,

Nu is a nucleophilic chemical entity comprising a  $\pi$  system, comprising an N, O or S atom or a chemical entity which is substituted with an N, O or S atom, [[.]]

wherein NuBB is linked to (AA)<sub>n</sub> or if n=0 to MABB via an amide bond and with the proviso, that when x=0, then n is at least 1,

and wherein the masked aldehyde may be transformed into a free aldehyde, and the free aldehyde group is capable of interacting intramolecularly with an amide group, thereby forming an N-acyliminium ion,

and wherein said N-acyliminium ion is capable of acting as an electrophile for intramolecular reaction with said nucleophilic chemical entity,

and wherein said precursor molecule is attached to a solid support.

84. (Currently amended) The method according to Claim 82, wherein the intramolecular nucleophilic reaction is a Pictet Spengler reaction.

85. (Currently amended) The method according to Claim 82, wherein transforming the masked aldehyde into a free aldehyde comprises acid treatment, alkaline treatment, fluoridolysis or hydrogenolysis.

Claims 86-91 (Cancelled)

92. (Original) The method according to claim 82, wherein said heterocyclic organic compound comprises 3 fused rings.

Claims 93-94 [Cancelled]

95. (Original) The method according to claim 92, wherein the heterocyclic organic compound comprises one ring derived from the nucleophile chemical entity.

96. (Cancelled)

97. (Original) The method according to claim 82, wherein ring A is a lactam.

Claims 98-106 (Cancelled)

107. (Currently amended) A method of preparing a heterocyclic organic compound comprising at least 2 fused rings designated A and B, wherein said method comprises the steps of

- a) performing the method according to ~~any of~~ claims 82 ~~to 106~~, thereby obtaining a heterocyclic organic compound comprising at least one carbonyl group; and
- b) deoxygenating the heterocyclic organic compound comprising at least one carbonyl group;
- c) thereby obtaining a heterocyclic organic compound comprising at least two fused rings.

108. (Currently amended) A method of preparing a library comprising at least 2 different cyclic organic compounds each comprising at least 2 fused rings designated A and B, wherein ring A is substituted with a carbonyl group and ring A and B shares at least one N atom, said method comprising the steps of

- a) Providing at least 2 different precursor molecules of the formula:  
[MABB-(AA)<sub>n</sub>-NuBB], wherein

MABB is a masked aldehyde building block of the formula:

[MA-L<sub>1</sub>-AG-], wherein

MA is a masked aldehyde,

L<sub>1</sub> is an aryl or alkyl comprising x covalently linked atoms selected from the group consisting of C, N, O and S, wherein x is an integer in the range of 0 to

10, and wherein said aryl ring or alkyl chain may be substituted independently on each position, and wherein the atom most proximal to the CO group is a carbon atom,

AG is an acidic group capable of forming an amide bond,

AA is an amino acid of the formula  $\text{-NHCR}^1\text{R}^2\text{CO-}$  and n is an integer in the range of 0 to 5,

NuBB is a nucleophile building block of the formula

$[\text{-NH-L}_2\text{-Nu-}]$ , wherein

-NH is an amino group that form an amide bond with AA or when n is 0 with AG,

L<sub>2</sub> is an alkyl comprising in the range of 1 to 4 covalently linked atoms selected from the group consisting of C, N, O and S, wherein each atom may be independently substituted,

Nu is a nucleophilic chemical entity comprising a  $\pi$  system,

wherein NuBB is linked to (AA)<sub>n</sub> or if n=0 to MABB via an amide bond and with the proviso, that when x=0, then n is at least 1,

and wherein the masked aldehyde may be transformed into a free aldehyde, and the free aldehyde group is capable of interacting intramolecularly with an amide group, thereby forming an N-acyliminium ion,

and wherein said N-acyliminium ion is capable of acting as an electrophile for intramolecular reaction with said nucleophilic chemical entity,

and wherein said precursor molecule is attached to a solid support[[.]],

b) performing the method according to ~~any of claims 82 to 106~~ for each of said precursor molecules

c) thereby obtaining a library comprising at least 2 different cyclic organic compounds.

109. (Currently amended) The method according to claim 108, wherein the precursor molecule is a precursor molecule ~~according to any of claims 1 to 58~~ of the formula

$[\text{MABB-(AA)}_n\text{-NuBB}]$ , wherein

MABB is a masked aldehyde building block of the formula:

[MA-L<sub>1</sub>-AG-], wherein

MA is a masked aldehyde,

L<sub>1</sub> is an aryl or alkyl comprising x covalently linked atoms selected from the group consisting of C, N, O and S, wherein x is an integer in the range of 0 to 10, and wherein said aryl ring or alkyl chain may be substituted independently on each position, and wherein the atom most proximal to the CO group is a carbon atom,

AG is an acidic group capable of forming an amide bond,

AA is an amino acid of the formula -NHCR<sup>1</sup>R<sup>2</sup>CO- and n is an integer in the range of 0 to 5,

NuBB is a nucleophile building block of the formula

[-NH-L<sub>2</sub>-Nu-], wherein

-NH is an amino group that form the amide bond with AA or when n is 0 with AG,

L<sub>2</sub> is an alkyl comprising in the range of 1 to 4 covalently linked atoms selected from the group consisting of C, N, O and S, wherein each atom may be independently substituted,

Nu is a nucleophilic chemical entity comprising a  $\pi$  system, comprising an N, O or S atom or a chemical entity which is substituted with an N, O or S atom,[[.]]

wherein NuBB is linked to (AA)<sub>n</sub> or if n=0 to MABB via an amide bond and with the proviso, that when x=0, then n is at least 1,

and wherein the masked aldehyde may be transformed into a free aldehyde, and the free aldehyde group is capable of interacting intramolecularly with an amide group, thereby forming an N-acyliminium ion,

and wherein said N-acyliminium ion is capable of acting as an electrophile for intramolecular reaction with said nucleophilic chemical entity,

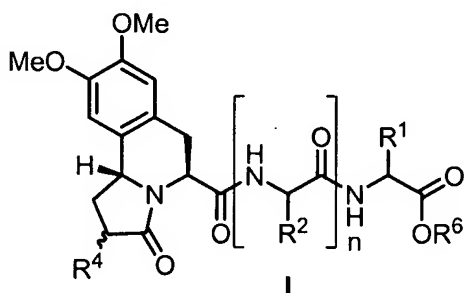
and wherein said precursor molecule is attached to a solid support.

Claims 110-113 (Cancelled)

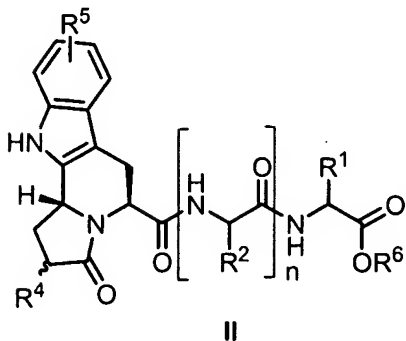
114 (Currently amended) Library of heterocyclic compounds, wherein said compounds comprises at least 2 fused rings designated A and B, wherein ring A is substituted with a carbonyl group and ring A and B shares at least one N atom, and wherein a sequence of one or more amino acids is covalently linked to said fused rings, wherein said library is prepared by the method according to ~~any of claims 108 to 113~~, and wherein said heterocyclic compounds are linked to a solid support.

115. (Cancelled)

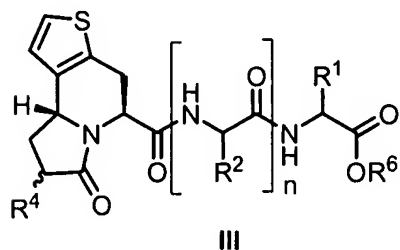
116. (Currently amended) The library according to ~~any of claims 114 and 115~~, wherein the library comprises or consists of compounds of the general formula:



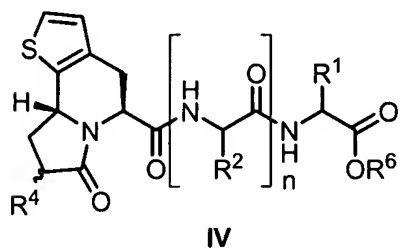
117. (Currently amended) The library according to ~~any of claims 114 and 115~~, wherein the library comprises or consists of compounds of the general formula:



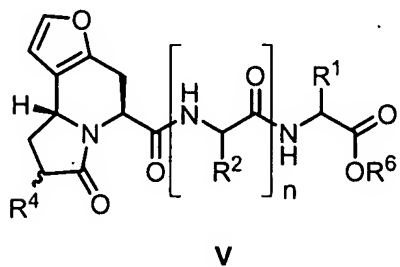
118. (Currently amended) The library according to ~~any of~~ claims 114 and ~~115~~, wherein the library comprises or consists of compounds of the general formula:



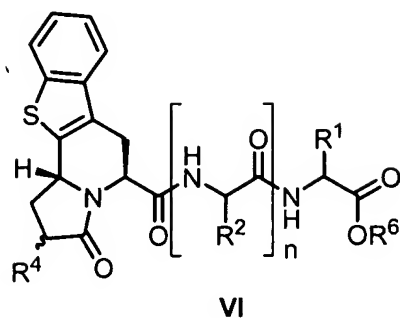
119. (Currently amended) The library according to ~~any of~~ claims 114 and ~~115~~, wherein the library comprises or consists of compounds of the general formula:



120. (Currently amended) The library according to ~~any of~~ claims 114 and ~~115~~, wherein the library comprises or consists of compounds of the general formula:



121. (Currently amended) The library according to ~~any of~~ claims 114 and ~~115~~, wherein the library comprises or consists of compounds of the general formula:



Claims 122-124 (Cancelled)

125. (Currently amended) A method of identifying a heterocyclic organic compound capable of associating with a cell surface molecule naturally expressed on the surface of a cell, said method comprising the steps of

- i) Providing the library according to ~~any of claims 114 and 128,~~
- ii) Providing a composition comprising said cell surface molecule,
- iii) Incubating said library with said composition
- iv) Identifying heterocyclic compounds of said library capable of specifically associating with said cell surface molecule.

Claims 126-133 (Cancelled)

134 (Currently amended) A method of treatment of a clinical condition comprising administering ~~Use of~~ a heterocyclic organic compound identified according to the method according to ~~any of claims 125 and 133 for the preparation of a medicament for the treatment of a clinical condition in~~ to an individual in need thereof.

Claims 135-138 [Cancelled]

139 (Currently amended) A method of identifying a heterocyclic organic compound capable of acting as a protease inhibitor, said method comprising the steps of

- i) Providing the library according to ~~any of claims 114 and 124,~~
- ii) Providing a peptide substrate of a protease,



**Int'l Appl. No.** : **PCT/DK2004/000454**  
**Int'l Filing Date** : **June 25, 2004**

- iii) Providing a protease capable of cleaving said substrate
- iv) Incubating said library with said peptide substrate and said protease
- v) Identifying heterocyclic compounds of said library capable of specifically inhibiting cleavage of said substrate.

Claims 140-143 (Cancelled)